

**WHAT IS CLAIMED IS:**

1. A method of preventing or reducing diarrhea and/or steatorrhea in an HIV-positive patient comprising administering a High Activity Antiretroviral drug and a  
5 buffered and enteric coated composition comprising an enzyme selected from the group consisting of: pancreatic proteases, lipases, co-lipases, nucleases, amylases and other bio-active substances produced by the pancreatic gland in an effective amount to prevent or reduce diarrhea and/or steatorrhea.
- 10 2. A method of preventing or reducing diarrhea and/or steatorrhea in an HIV-positive patient associated with the treatment of with High Activity Antiretroviral drugs which comprise of protease inhibitors, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors or a combination thereof, comprising the steps of:
  - 15 a) administering to said HIV-positive patient a drug comprising a protease inhibitor, a nucleoside reverse transcriptase inhibitor, a non-nucleoside reverse transcriptase inhibitor, or a combination thereof contained in a pharmaceutically acceptable vehicle;
  - b) administering simultaneously or subsequently to said High Activity  
20 Antiretroviral drugs, a buffered and enteric-coated composition comprising:
    - of from about 10 to about 90% of an enzyme selected from the group consisting of pancreatic proteases, lipases, co-lipases, co-enzymes, nucleases, amylases and other bio-active substances produced by the pancreatic gland;
    - of from about 15 to about 60% of a buffering agent selected from the  
25 group consisting of: anhydrous sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate, ammonium carbonate, tromethamine, di(tris)hydroxymethyl-aminomethane carbonate, tris-glycine, di-arginine, tri-arginine, poly-arginine, di-lysine, tri-lysine, poly-lysine, diethylamine and triethanolamine, said buffering agent providing a pH of from 7 to 9 in the small intestine of a patient, and  
30 said lipase having an activity of from about 24% to about 100% at said pH of from 7 to 9;

of from about 0.5 to about 16% w/w of a disintegrant selected from the group consisting of ursodiol, starch, modified starches, microcrystalline cellulose and propylene glycol alginate;

5 of from about 1 to about 19% w/w of an adhesive polymer selected from the group consisting of polyvinylpyrrolidone, hydroxyethyl cellulose, cellulose acetate phthalate, ethyl cellulose and hydroxypropylmethyl cellulose; and

10 of from about 7 to about 15 % w/w of a non-porous, gastric acid-resistant and pharmaceutically acceptable polymer coating which contains less than 2% talc and which is insoluble in the pH range of from about 1.5 to about 5 but is soluble in the pH range of about 5.5 to about 9, said polymer coating comprises a polymer selected from the group consisting of hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, diethyl phthalate, dibutyl phthalate, enteric coating polymer dispersion, and an acrylic based polymeric dispersion.

15 3. The method of claim 2 wherein said protease inhibitor is selected from the group consisting of: indinavir sulfate, amprenavir, ritonavir, saquinavir, nelfinavir mesylate, and saquinavir mesylate.

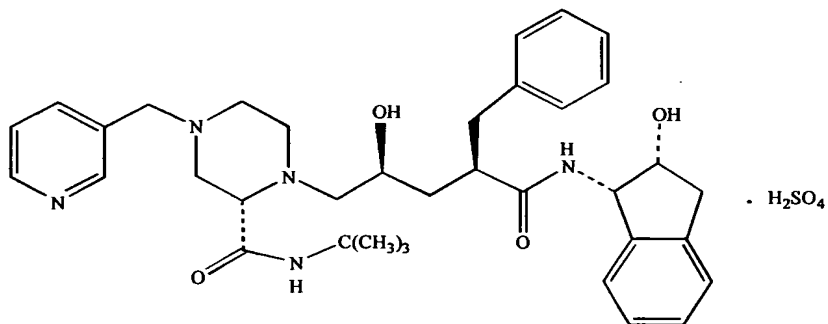
20 4. The method of claim 2 wherein said nucleoside reverse transcriptase inhibitor is selected from the group consisting of: zalcitabine, stavudine, zidovudine, lamivudine, lamivudine/zidovudine combo and didanosine.

25 5. The method of claim 2 wherein said non-nucleoside reverse transcriptase inhibitor is selected from the group consisting of: efavirenz, nevirapine, abacavir sulfate, and delavirdine mesylate.

6. The method of claim 2 wherein said bicarbonate-buffered and enteric-coated compositions comprising of from about 10 to 90% of an enzyme selected from the group consisting of pancreatic proteases, lipases, co-lipases, nucleases, amylases and 30 other bio-active substances produced by the pancreatic gland.

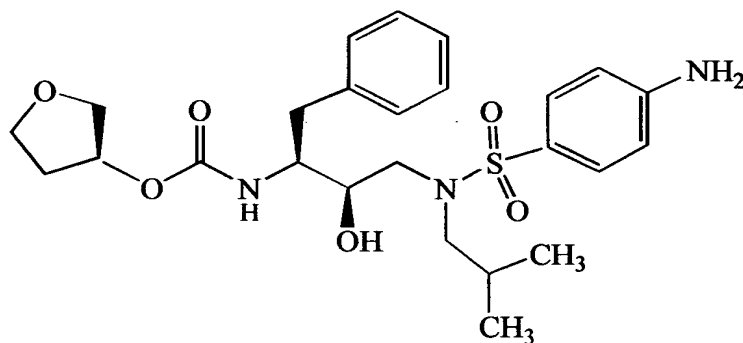
7. The method of claim 2 wherein said co-enzyme is a co-lipase.

8. The method of claim 3 wherein said indinavir sulfate has the formula:

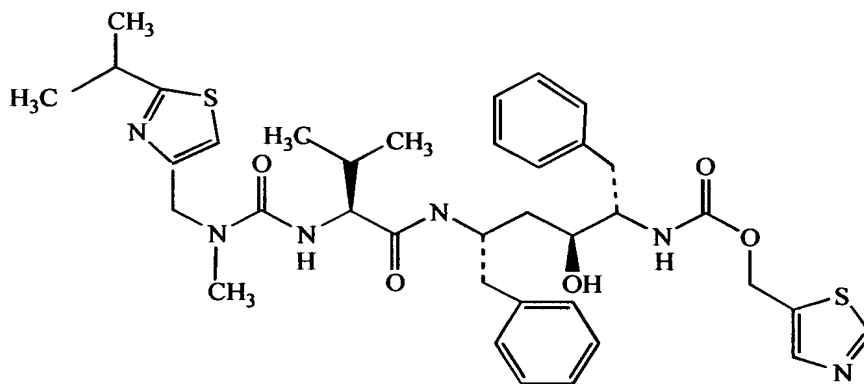


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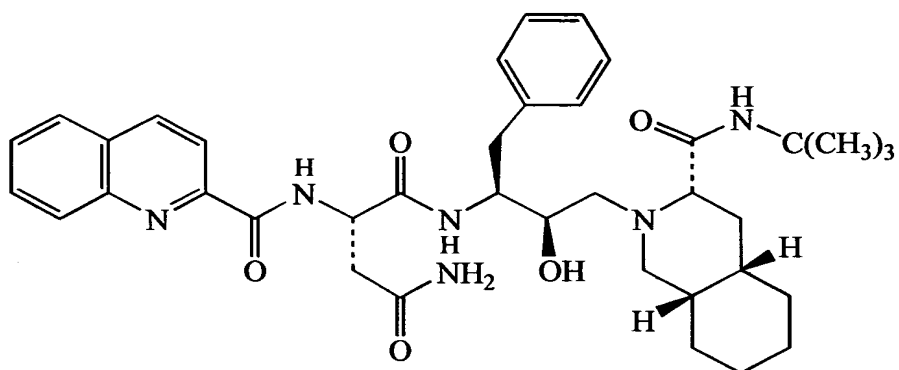
9. The method of claim 3 wherein said amprenavir has the formula:



10. The method of claim 3 wherein said ritonavir has the formula:

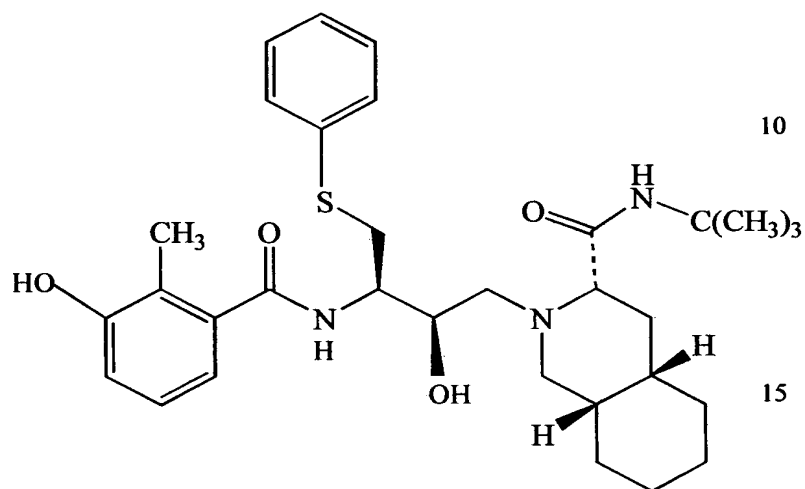


11. The method of claim 3 wherein said saquinavir has the formula:



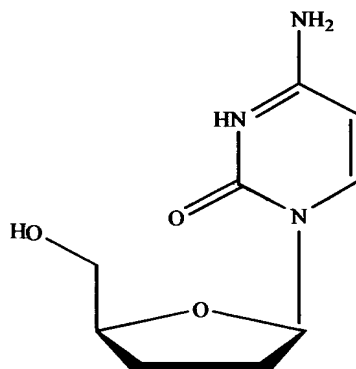
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12. The method of claim 3 wherein said nelfinavir has the formula:

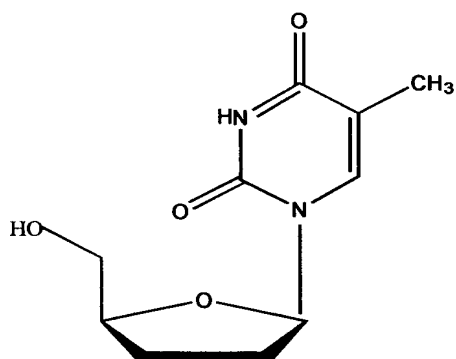


- 20 13. The method of claim 4 wherein said zalcitabine has the formula:

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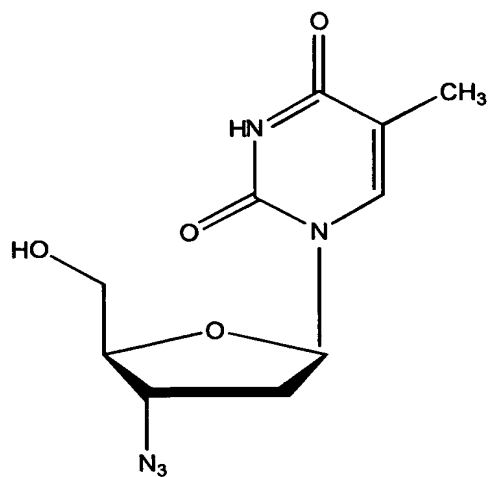


- 5 14. The method of claim 4 wherein said stavudine has the formula:

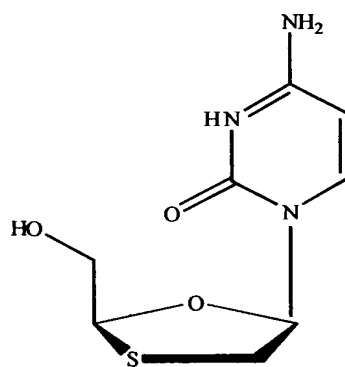


15. The method of claim 4 wherein said zidovudine has the formula:

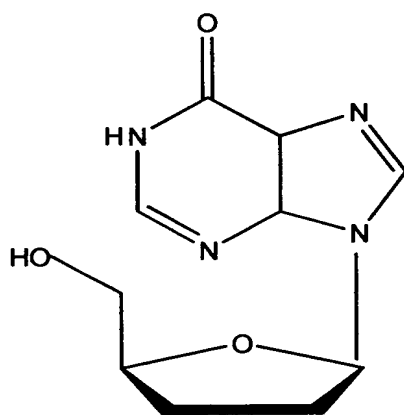
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16. The method of claim 4 wherein said lamivudine has the formula



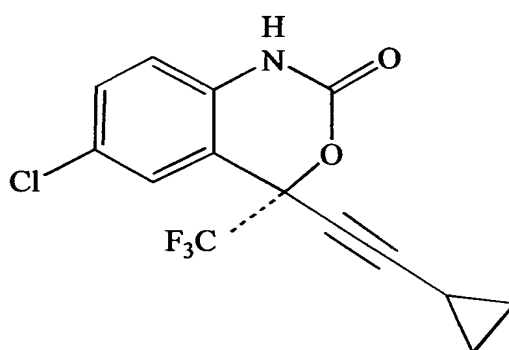
17. The method of claim 4 wherein didanosine has the formula:



18. The method of claim 5 wherein said efavirenz has the formula:

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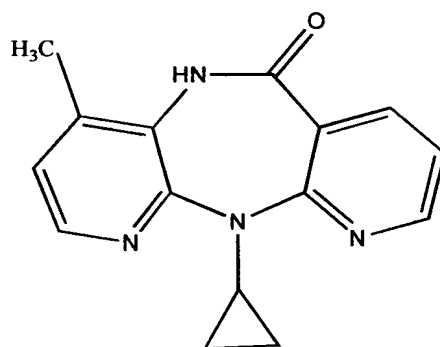
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- 15 19. The method of claim 5 wherein said nevirapine has the formula:

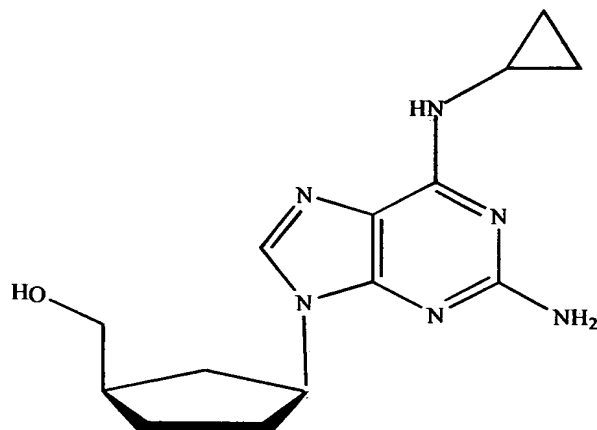
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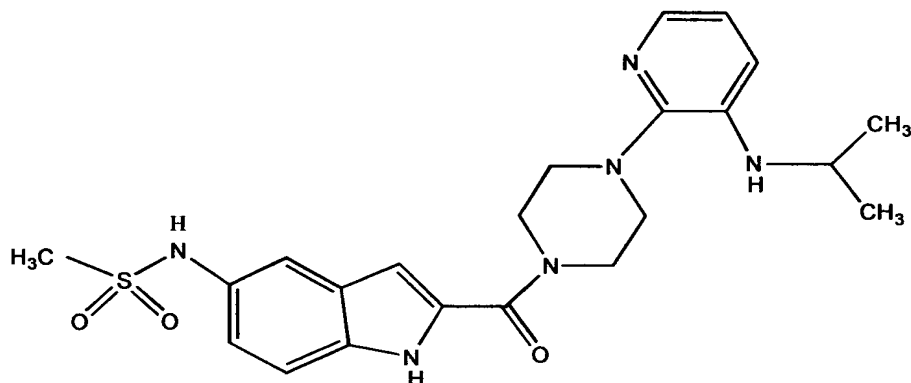
20. The method of claim 5 wherein said abacavir has the formula:

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21. The method of claim 5 wherein said delavirdine has the formula:



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22. A composition for preventing or reducing diarrhea and/or steatorrhea in HIV-positive patients treated with High Activity Antiretroviral drugs comprising:

20 a protease inhibitor, a nucleoside reverse transcriptase inhibitor, a non-nucleoside reverse transcriptase inhibitor, or a combination thereof contained in a pharmaceutically acceptable vehicle;

a buffered and enteric-coated composition comprising:

of from about 10 to about 90% of an enzyme selected from the group consisting of pancreatic proteases, lipases, co-lipases, nucleases, amylases and other bio-active substances produced by the pancreatic gland;



of from about 15 to about 60% of a buffering agent selected from the group consisting of: anhydrous sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate, ammonium carbonate, tromethamine, di(tris)hydroxymethyl-aminomethane carbonate, tris-glycine, di-arginine, tri-arginine, poly-arginine, di-lysine, tri-lysine, poly-lysine, diethylamine and triethanolamine, said buffering agent providing a pH of from 7 to 9 in the small intestine of a patient, and said lipase having an activity of from about 24% to about 100% at said pH of from 7 to 9;

of from about 0.5 to about 16% w/w of a disintegrant selected from the group consisting of ursodiol, starch, modified starches, microcrystalline cellulose and propylene glycol alginate;

of from about 1 to about 19% w/w of an adhesive polymer selected from the group consisting of polyvinylpyrrolidone, hydroxyethyl cellulose, cellulose acetate phthalate, ethyl cellulose and hydroxypropylmethyl cellulose; and

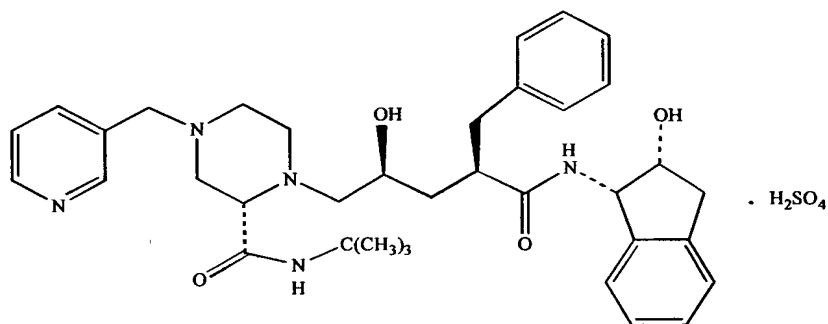
of from about 7 to about 15% w/w of a non-porous, gastric acid-resistant and pharmaceutically acceptable polymer coating which contains less than 2% talc and which is insoluble in the pH range of from about 1.5 to about 5 but is soluble in the pH range of about 5.5 to about 9, said polymer coating comprises a polymer selected from the group consisting of hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, diethyl phthalate, dibutyl phthalate, enteric coating polymer dispersion, and an acrylic based polymeric dispersion.

23. The composition of claim 22 wherein said protease inhibitor is selected from the group consisting of: indinavir sulfate, amprenavir, ritonavir, saquinavir, nelfinavir mesylate, and saquinavir mesylate.

24. The composition of claim 22 wherein said nucleoside reverse transcriptase inhibitor is selected from the group consisting of: zalcitabine, stavudine, zidovudine, lamivudine, lamivudine/zidovudine combo and didanosine.

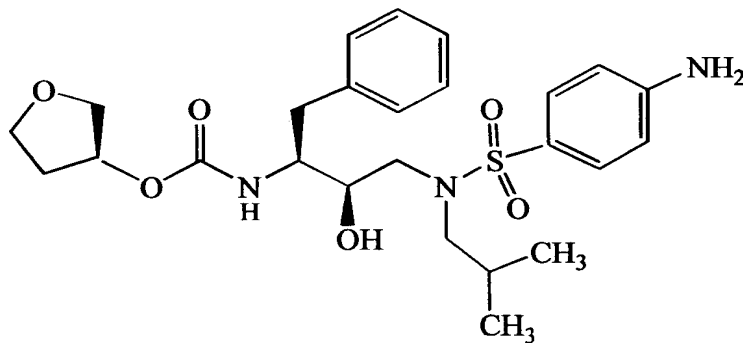
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25. The composition of claim 22 wherein said non-nucleoside reverse transcriptase inhibitor is selected from the group consisting of: efavirenz, nevirapine, abacavir sulfate, and delavirdine mesylate.
- 5 26. The composition of claim 22 wherein said bicarbonate-buffered and enteric-coated compositions comprising of from about 10 to 90% of an enzyme selected from the group consisting of pancreatic proteases, lipases, co-lipases, nucleases, amylases and other bio-active substances produced by the pancreatic gland.
- 10 27. The composition of claim 22 wherein said co-enzyme is a co-lipase.
28. The composition of claim 23 wherein said indinavir sulfate has the formula:

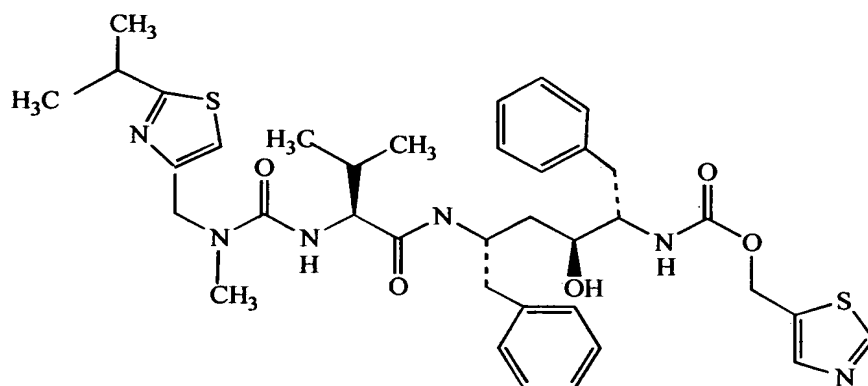


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29. The composition of claim 23 wherein said amprenavir has the formula:

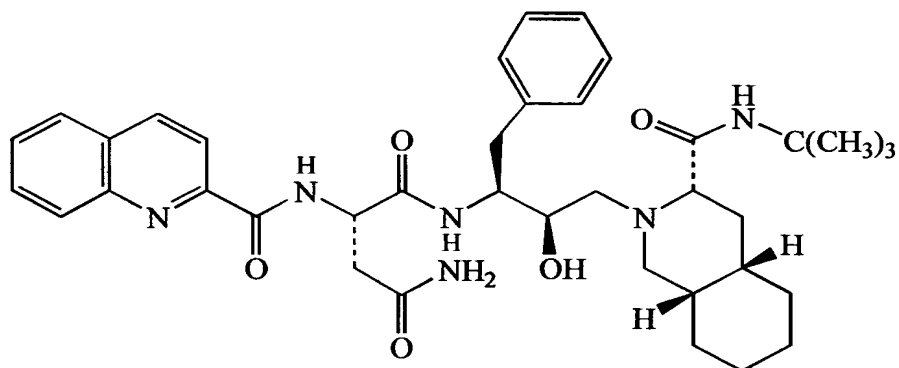


30. The composition of claim 23 wherein said ritonavir has the formula:



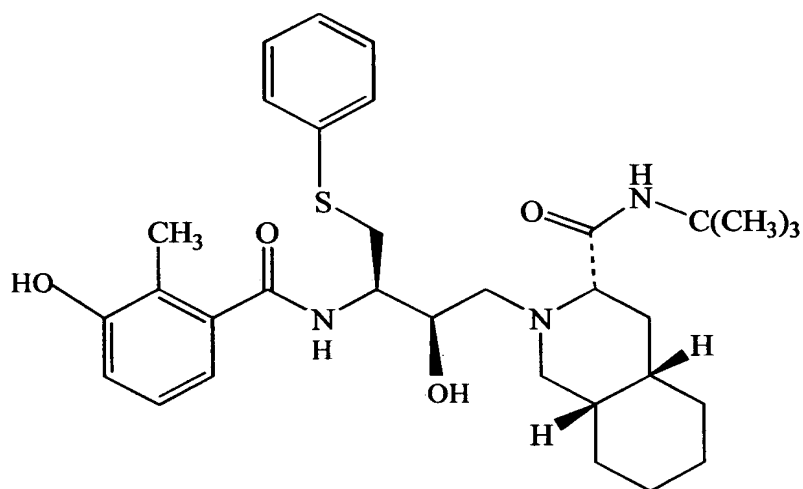
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31. The composition of claim 23 wherein said saquinavir has the formula:



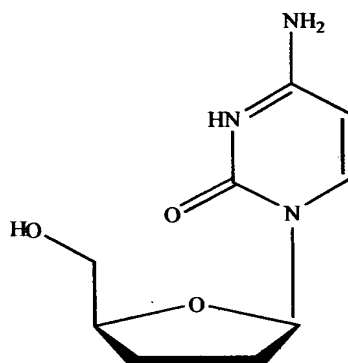
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32. The composition of claim 23 wherein said nelfinavir has the formula:



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33. The composition of claim 24 wherein said zalcitabine has the formula:



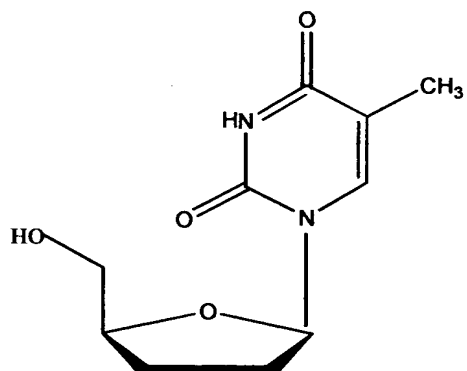
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34. The composition of claim 24 wherein said stavudine has the formula:

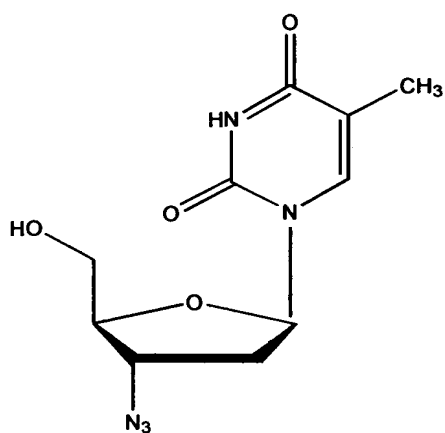
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10 35. The composition of claim 24 wherein said zidovudine has the formula:

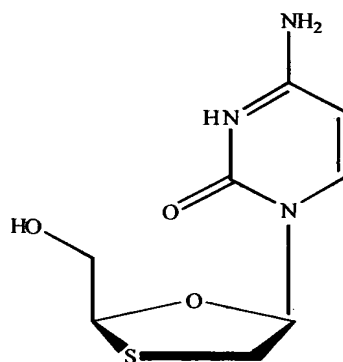
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36. The composition of claim 24 wherein said lamivudine has the formula

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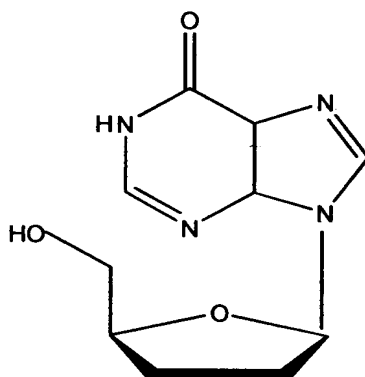


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37. The composition of claim 24 wherein didanosine has the formula:

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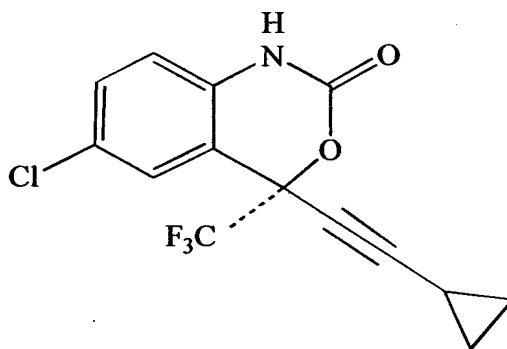


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38. The composition of claim 25 wherein said efavirenz has the formula:

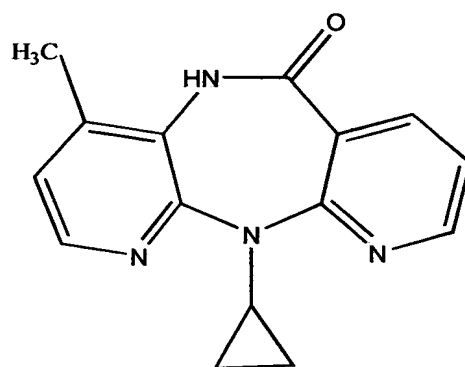
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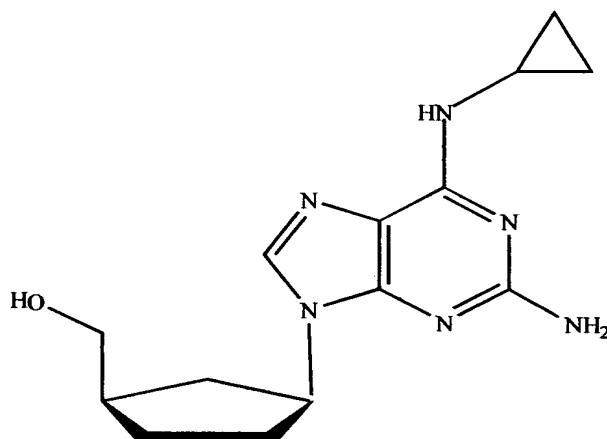
39. The composition of claim 25 wherein said nevirapine has the formula:

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10 40. The composition of claim 25 wherein said abacavir has the formula:

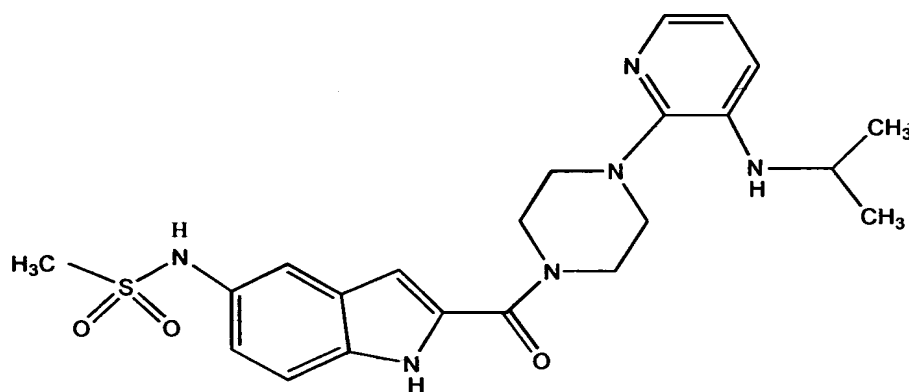
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41. The composition of claim 25 wherein said delavirdine has the formula:



42. A composition for preventing or reducing diarrhea and/or steatorrhea in HIV-  
positive patients treated with High Activity Antiretroviral drugs comprising:

a protease inhibitor, a nucleoside reverse transcriptase inhibitor, a non-nucleoside reverse transcriptase inhibitor, or a combination thereof contained in a pharmaceutically acceptable vehicle;

a buffered and enteric-coated composition comprising:

of from about 10 to about 90% of co-lipase produced by the pancreatic gland;

of from about 15 to about 60% of a buffering agent selected from the group consisting of: anhydrous sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate, ammonium carbonate, tromethamine, di(tris)hydroxymethyl-aminomethane carbonate, tris-glycine, di-arginine, tri-arginine, poly-arginine, di-lysine, tri-lysine, poly-lysine, diethylamine and triethanolamine, said buffering agent providing a pH of from 7 to 9 in the small intestine of a patient;

of from about 0.5 to about 16% w/w of a disintegrant selected from the group consisting of ursodiol, starch, modified starches, microcrystalline cellulose and propylene glycol alginate;

of from about 1 to about 19% w/w of an adhesive polymer selected from the group consisting of polyvinylpyrrolidone, hydroxyethyl cellulose, cellulose acetate phthalate, ethyl cellulose and hydroxypropylmethyl cellulose; and



of from about 7 to about 15% w/w of a non-porous, gastric acid-resistant and pharmaceutically acceptable polymer coating which contains less than 2% talc and which is insoluble in the pH range of from about 1.5 to about 5 but is soluble in the pH range of about 5.5 to about 9, said polymer coating comprises a polymer  
 5 selected from the group consisting of hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, diethyl phthalate, dibutyl phthalate, enteric coating polymer dispersion, and an acrylic based polymeric dispersion.

43. A composition for correcting fat malabsorption and loss of body mass  
 10 associated with diarrhea and/or steatorrhea in HIV-positive patients treated with High Activity Antiretroviral drugs comprising:

a protease inhibitor, a nucleoside reverse transcriptase inhibitor, a non-nucleoside reverse transcriptase inhibitor, or a combination thereof in a pharmaceutically acceptable vehicle;

15 a buffered and enteric-coated composition comprising:

of from about 10 to about 90% of co-lipase produced by the pancreatic gland;

of from about 15 to about 60% of a buffering agent selected from the group consisting of: anhydrous sodium carbonate, sodium bicarbonate, potassium  
 20 carbonate, potassium bicarbonate, ammonium carbonate, tromethamine, di(tris)hydroxymethyl-aminomethane carbonate, tris-glycine, di-arginine, tri-arginine, poly-arginine, di-lysine, tri-lysine, poly-lysine, diethylamine and triethanolamine, said buffering agent providing a pH of from 7 to 9 in the small intestine of a patient;

of from about 0.5 to about 16% w/w of a disintegrant selected from the  
 25 group consisting of ursodiol, starch, modified starches, microcrystalline cellulose and propylene glycol alginate;

of from about 1 to about 19% w/w of an adhesive polymer selected from the group consisting of polyvinylpyrrolidone, hydroxyethyl cellulose, cellulose acetate phthalate, ethyl cellulose and hydroxypropylmethyl cellulose; and

30 of from about 7 to about 15% w/w of a non-porous, gastric acid-resistant and pharmaceutically acceptable polymer coating which contains less than 2% talc and which is insoluble in the pH range of from about 1.5 to about 5 but is soluble

in the pH range of about 5.5 to about 9, said polymer coating comprises a polymer selected from the group consisting of hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, diethyl phthalate, dibutyl phthalate, enteric coating polymer dispersion, and an acrylic based polymeric dispersion.

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44. A method for correcting fat malabsorption and loss of body mass associated with diarrhea and/or steatorrhea in HIV-positive patients treated with High Activity Antiretroviral drugs which comprise of protease inhibitors, nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors or a combination thereof, comprising the steps of:

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a) administering to said HIV-positive patient a drug comprising a protease inhibitor, a nucleoside reverse transcriptase inhibitor, a non-nucleoside reverse transcriptase inhibitor, or a combination thereof contained in a pharmaceutically acceptable vehicle;

15

b) administering simultaneously or subsequently to said High Activity Antiretroviral drugs, a buffered and enteric-coated composition comprising:

of from about 10 to about 90% of an enzyme selected from the group consisting of pancreatic proteases, lipases, co-lipases, co-enzymes, nucleases, amylases and other bio-active substances produced by the pancreatic gland;

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of from about 15 to about 60% of a buffering agent selected from the group consisting of: anhydrous sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate, ammonium carbonate, tromethamine, di(tris)hydroxymethyl-aminomethane carbonate, tris-glycine, di-arginine, tri-arginine, poly-arginine, di-lysine, tri-lysine, poly-lysine, diethylamine and triethanolamine, said buffering agent providing a pH of from 7 to 9 in the small intestine of a patient, and said lipase having an activity of from about 24% to about 100% at said pH of from 7 to 9;

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of from about 0.5 to about 16% w/w of a disintegrant selected from the group consisting of ursodiol, starch, modified starches, microcrystalline cellulose and propylene glycol alginate;

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of from about 1 to about 19% w/w of an adhesive polymer selected from the group consisting of polyvinylpyrrolidone, hydroxyethyl cellulose, cellulose acetate phthalate, ethyl cellulose and hydroxypropylmethyl cellulose; and

5 of from about 7 to about 15 % w/w of a non-porous, gastric acid-resistant and pharmaceutically acceptable polymer coating which contains less than 2% talc and which is insoluble in the pH range of from about 1.5 to about 5 but is soluble in the pH range of about 5.5 to about 9, said polymer coating comprises a polymer selected from the group consisting of hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, diethyl phthalate, dibutyl phthalate, enteric coating polymer  
10 dispersion, and an acrylic based polymeric dispersion.

45. The method of claim 44 wherein said protease inhibitor is selected from the group consisting of: indinavir sulfate, amprenavir, ritonavir, saquinavir, nelfinavir mesylate, and saquinavir mesylate.

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46. The method of claim 44 wherein said nucleoside reverse transcriptase inhibitor is selected from the group consisting of: zalcitabine, stavudine, zidovudine, lamivudine, lamivudine/zidovudine combo and didanosine.

20 47. The method of claim 44 wherein said non-nucleoside reverse transcriptase inhibitor is selected from the group consisting of: efavirenz, nevirapine, abacavir sulfate, and delavirdine mesylate.

48. The method of claim 44 wherein said bicarbonate-buffered and enteric-coated  
25 compositions comprising of from about 10 to 90% of an enzyme selected from the group consisting of pancreatic proteases, lipases, co-lipases, nucleases, amylases and other bio-active substances produced by the pancreatic gland.